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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/624,670	07/24/2000	Pradip Mukerji	6407.US.p2	7619

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STEVEN F. WEINSTOCK  
ABBOTT LABORATORIES  
100 ABBOTT PARK ROAD  
DEPT. 377/AP6A  
ABBOTT PARK, IL 60064-6008

EXAMINER

RAMIREZ, DELIA M

ART UNIT PAPER NUMBER

1652

DATE MAILED: 02/24/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Advisory Action</b>	<b>Application No.</b> 09/624,670	<b>Applicant(s)</b> MUKERJI ET AL.	
	<b>Examiner</b> Delia M. Ramirez	<b>Art Unit</b> 1652	

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 20 January 2003 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY [check either a) or b)]**

- a) ☐ The period for reply expires \_\_\_\_\_ months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. **ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).**

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☒ A Notice of Appeal was filed on 22 September 2003. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☐ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
  - (b) ☐ they raise the issue of new matter (see Note below);
  - (c) ☐ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: \_\_\_\_\_.

3. ☐ Applicant's reply has overcome the following rejection(s): \_\_\_\_\_.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☒ affidavit, b) ☒ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: see attached.
6. ☐ ~~The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.~~
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☐ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: 1,3-5,24 and 47.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 50-53.

Claim(s) withdrawn from consideration: 6-7,25-46,49.

8. ☐ The drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_.
10. ☐ Other: \_\_\_\_\_

***ADVISORY ACTION***

1. Claims 1, 3-47, 49-53 are pending.
2. The request for reconsideration under 37 CFR 1.116, submission of a Declaration by Inventor Amanda E. Leonard, submission of alignments and references by Leonard et al., Qi et al. (2003), Zhang et al., and Qi et al. (2002) in reply to the Advisory Action mailed on 10/9/2003 are acknowledged. The submissions and Declaration have been considered. However, they are not deemed sufficient to place the application in condition for allowance for the following reasons.
3. Applicants argue that the Declaration by Inventor Amanda Leonard establishes a correlation between structure and function in connection with known elongases, therefore supporting the 70% similarity and 60% identity limitations in the claims. In particular, Applicants submit that the Leonard Declaration establishes the region of known elongases which is critical for the protein to properly function as an enzyme which adds two carbon atoms to the substrate. As such, it is Applicant's conclusion that the rejection of claims 50-53 under 35 USC 112, first paragraph has been overcome and should be withdrawn.
4. Applicant's arguments have been fully considered but are not deemed persuasive to overcome the rejection. The Leonard Declaration as well as the alignments and references submitted appear to suggest that there is a highly conserved motif (histidine rich motif), an ER retention signal, and some conserved residues according to the alignments of other elongases. The references cited appear to suggest that alterations in those conserved residues may cause reduction in enzyme activity or even inactivation. The declaration also submits that there are approximately 130 amino acids between the first conserved amino acid and the last conserved residue, which is labeled "core region", and indicates that there is little conservation over the remaining residues (outside the core region). While the information provided in the Declaration and the references cited does indicate certain structural elements which may be correlated

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with function, it is noted that (1) the claims as written do not recite additional structural limitations other than the % similarity/identity to the polypeptides of SEQ ID NO: 63-64, and (2) the highly conserved histidine motif is only a small fragment of the entire structure of the polypeptides of SEQ ID NO: 63 (292 amino acids) and 64 (299 amino acids). As shown in the alignments of Figure 3 provided by Applicants, the region corresponding to the histidine motif is 28 residues long. While it is agreed that there is a high % sequence homology in that region of 28 amino acids between the elongases of the instant application and other elongases, this motif represents at most 10% of the entire structure of the polypeptides of SEQ ID NO: 63-64. In regard to the conserved amino acids indicated in the declaration, it is noted that Figure 4 of the reference by Leonard et al. (Progress in Lipid Research 43:36-54, 2004) shows an alignment of several members of the ELO family where it is clear that a very small number of residues are highly conserved or identical (approximately 30 residues) in the so called "core region" of approximately 130 amino acids, therefore there is a substantial amount of variation within the "core region" (approximately 100 amino acids). Furthermore, as indicated by the Leonard Declaration, there is little conservation among the residues outside the core region. If an elongase is on average 260 amino acids long, in addition to the variability within the 130 amino acid "core region", there is also variability in the remaining half of the elongase structure. It is also noted that neither the specification nor the art provide any information as to (1) whether the histidine rich motif is the only structural element required for elongase activity, (2) the correlation between the highly conserved residues and function/substrate specificity except for those where it is known that substitutions lead to reduced activity as shown by Qi et al. (FEBS Letters 547:137-139, 2003), and (3) the correlation between those variable amino acids within the histidine motif and function/substrate specificity. Thus, in view of the lack of information as to a correlation between a substantial portion of the structure of an elongase and function, and the unpredictability of the art in regard to accurately assigning function based on structural homology, one of

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skill in the art cannot reasonably conclude that the specification is enabling for the full scope of the claims.

5. The rejections previously applied are, therefore, maintained for the reasons of record.

6. For purposes of Appeal, the status of the claims is as follows:

Claim(s) allowed: 1, 3-5, 8-24, and 47

Claims(s) objected to: NONE

Claim(s) rejected: 50-53

Claim(s) withdrawn from consideration: 6-7, 25-46, 49


7. Certain papers related to this application may be submitted to Art Unit 1652 by facsimile transmission. The FAX number is (703) 872-9306. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 CFR 1.6(d)). NOTE: If Applicant submits a paper by FAX, the original copy should be retained by Applicant or Applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED, so as to avoid the processing of duplicate papers in the Office.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Delia M. Ramirez whose telephone number is (571) 272-0938. The examiner can normally be reached on Monday-Friday from 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Ponnathapura Achutamurthy can be reached on (571) 272-0928. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-1234.

Delia M. Ramirez, Ph.D.  
Patent Examiner  
Art Unit 1652

DR  
February 13, 2004

  
REBECCA E. PROUTY  
PRIMARY EXAMINER  
GROUP 1808-  
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